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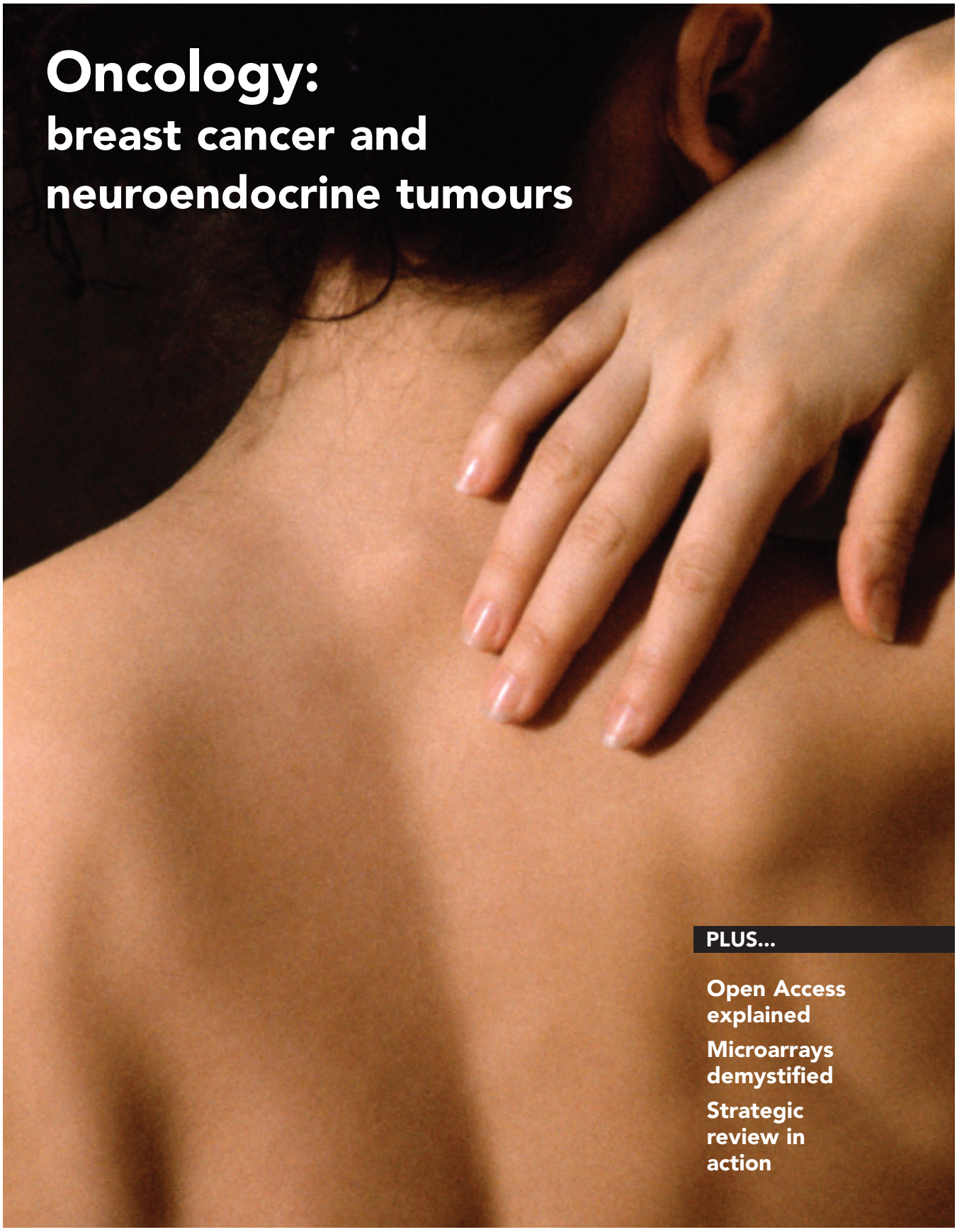
THE NEWSLETTER OF THE SOCIETY FOR ENDOCRINOLOGY NUMBER 73 • AUTUMN 2004

THE Endocrinologist



Oncology:
breast cancer and neuroendocrine tumours

PLUS...

Open Access explained

Microarrays demystified

Strategic review in action

The Endocrinologist

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Deadline for news items for the Winter 2004 issue: **20 October 2004**.
Please send contributions to the above address.

EDITORIAL

The 2004 Olympics are a mere memory, and the long hazy, rainy days of summer have given way to a new academic year. There are new students, new teaching, new reports to write to top up the filing cabinets and a new (personal) resolution not to get completely submerged in bureaucratic paper pushing.

Transparency has become a buzzword in education and management so, to follow suit, *The Endocrinologist* is throwing open it's doors onto the activities of the Society. We hope that regular features about your Society will encourage new members to get involved in the shaping of things to come. This issue includes a brief overview of the Society's wide-ranging committee activities (page 4-5) and, following the strategic review for 2004-2009, you can also find out about the business plan, projected activities and strategy for the next 5 years (page 5). We always welcome correspondence from our members about any issue relating to the Society for Endocrinology and, if these are not too ... well ... defamatory, we shall be happy to publish them.

This year's November meeting is just around the corner. To complement the oncology symposia, we have included two related articles in this issue. On page 12, Anthony Howell explains why aromatase inhibitors are challenging tamoxifen as the next leading treatment for breast cancer. Meanwhile, on page 10-11, you can read Martyn Caplin's extensive update on the rare gastroenteropancreatic endocrine tumours.

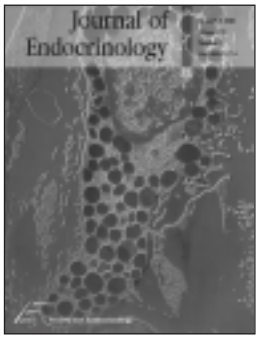
Steve Byford, Publishing Director at the Society, argues the case for and against Open Access journals and the implications for the Society. Will it come down to pay and display (web not windscreen) and who is going to pay? In considering our own Society Steve concludes that " ... Open Access paradise is visible to us in the distance, but in order to get there we have to cross a bottomless ravine using an unsafe rope bridge". Scary, but read the article and please contribute your views.

Finally we have a taste of home Olympics. Hotspur is obviously still in training to outrun Kelly Holmes, but at least his G-registration has ensured that he finished several sponsored runs including a half marathon. He did not quite reach the world record time for the over eighties or out-run a banana, but his efforts for fundraising and completing a speech in a personal best time are commendable. Catch up with his exploits on page 13.

I'm sure I don't need to remind you that the November meeting is the next highlight on your calendar. It takes place on 1-3 November at the Royal College of Physicians in London. I look forward to seeing you all there.

SAFFRON WHITEHEAD

‘Starling’ work!



In 1905, Ernest Henry Starling first assigned the term hormone to ‘the chemical messengers which, speeding from cell to cell along the blood stream, may co-ordinate the activities and growth of different parts of the body’ (*Lancet*, 5 August 1905, 339-341).

Journal of Endocrinology is commemorating this remarkable centenary with a series of *Starling reviews*, topical articles highlighting the role of endocrinology as a biomedical speciality, as well as its impact on global health and well-being. A review will be published in each issue during 2005, focusing on progress in endocrinology, both achieved and anticipated.

The *Starling review* series will start in the January issue with a biography of Ernest Henry Starling by John Henderson (St George’s Hospital Medical School, London) and an article on hypothalamic releasing factors by Nobel Laureate Roger Guillemin (Salk Institute for Biological Studies, La Jolla, California). Other reviews in the series will include ‘Appetite control’ by Steve Bloom (Imperial College, London), ‘Behaviour’ by Donald Pfaff (Rockerfeller Laboratory of Neurobiology and Behaviour, New York), and ‘HRT: from monkey glands to transdermal patches’ by Susan Davis (Jean Hailes Research Unit, Clayton, Victoria, Australia).

Impact on the increase

Once again, Society journals have shown healthy increases in their all-important impact factors. *Endocrine-Related Cancer* leapt spectacularly from 6.087 to 8.894, *Journal of Endocrinology* has for the first time topped three, jumping from 2.879 to 3.023, and our official clinical journal *Clinical Endocrinology* (published by Blackwell Publishing) has risen from 2.674 to 2.767. *Journal of Molecular Endocrinology* jumped to its highest ever value last year, and this year has shown only a very modest fall. These impact factors are a measure of how many times papers published in 2001 and 2002 were cited in 2003.

Endocrine-Related Cancer’s success gives it the second highest impact factor of all 88 endocrinology and metabolism journals listed in ISI’s *Journals Citation Report*. Meanwhile, the value for *Journal of Endocrinology* means that it continues its run of yearly increases since 1997.

Travel grants

Up to £500 is available to members to assist with travel expenses.

If you earn less than £30 000 (excluding London weighting) or you are a clinical fellow not in receipt of any other funding, in any 12 month period you are eligible to apply for a grant to attend:

- the BES meeting
- the Molecular Endocrinology Workshop at Summer School
- the Society’s November meeting
- and one endocrine-related overseas conference

Grant applications are considered three times per year as follows:

- 15 January – for overseas conferences and the BES 2005 meeting
- 15 April – for overseas conferences and the Molecular Endocrinology Workshop
- 15 August – for overseas conferences and the Society’s November meeting
- Grants for lab visits and clinical departmental visits

In addition, young endocrinologist members (aged less than 35 years and no more than 6 years post MD/MRCP) can obtain grants to visit:

- labs to gain experience
- clinical departments outside their Calman rotation

Up to £500 is available for lab visits within the UK and Europe, and up to £1000 for other locations. Up to £500 is available for UK-based clinical departmental visits and up to £1000 for Europe-based departmental visits.

All grants are jointly funded by the Society for Endocrinology and the Clinical Endocrinology Trust.

New officers

Following our call for nominations for new Society officers last May, one proposal was received from the membership for each of the three posts. We are therefore pleased to announce that **Professor John Wass** (Oxford) will become Chairman, **Professor Julia Buckingham** (London) is to be General Secretary, and that the Programme Secretary will be **Dr David Ray** (Manchester). They will all take office from November 2005 for a period of 3 years. **Professor Anne White** will commence the fourth year of her 5-year period as Treasurer in November 2004; nominations for this post will be sought in 2005.

Diploma update

Given the other forms of recognition available for endocrine clinicians, the Clinical Committee has concluded that there is no current need for the Society to introduce a clinical diploma in endocrinology. This follows several enquiries that were received after the recent launch of a postgraduate diploma in endocrinology for scientists.

SOCIETY CALENDAR

1-3 November 2004
195th Meeting of the Society for Endocrinology
Royal College of Physicians, London, UK
(see advert on page 9)

16 February 2005
Society for Endocrinology Clinical Cases Meeting
The Royal Society, London, UK
Cases deadline: 20 October 2004

4-6 April 2005
24th Joint Meeting of the British Endocrine Societies
Harrogate International Centre, Harrogate, UK
Abstract deadline: 12 November 2004

5-8 July 2005
Society for Endocrinology Summer School
St Aidan’s College, Durham, UK
(see advert on page 5)

30 August-1 September 2005
Society for Endocrinology Endocrine Nurses Training Course
John Macintyre Centre, Edinburgh, UK

7-9 November 2005
196th Meeting of the Society for Endocrinology
Royal College of Physicians, London, UK

Your Society needs you!

Eight diverse committees provide an opportunity for you, the members, to play a part in shaping your Society and, indeed, the future of endocrinology. Their latest activities are reported in a new, regular news feature below. But if you're unclear about what they do, and how you could get involved, then read on...

Awards Committee *(Chair: Paul Stewart, Birmingham)*
- oversees the selection of Society medallists, fellowships and Young Endocrinologists review lecturers
- nominates Society members for consideration by the Government for UK Honours

BES Committee *(Chair: John Connell, Glasgow)*
- sets policy for BES meetings
- associated Programme Organising Committee sets BES scientific programmes
- comprises representatives from each BES constituent society

Clinical Committee *(Chair: Michael Sheppard, Birmingham)*
- responds to ethical issues
- leads in developing guidelines for management of endocrine disorders
- runs a programme of meetings (including the Advanced Endocrine Course and Clinical Practice Day at Summer School)
- makes suggestions to Programme Committees for the Society and BES meetings

Finance Committee *(Chair: Anne White (Society Treasurer), Manchester)*
- advises Council on financial strategy
- monitors investments, income and expenditure
- recommends budgets

Nurse Committee *(Chair: Maggie Carson, Edinburgh)*
- provides a communication network for endocrine nurses
- has a leading role in developing guidelines for best nursing practice
- organises an annual training course and nurse sessions at the November and BES meetings

Programme Committee *(Chair: Ann Logan (Programme Secretary), Birmingham)*
- organises Society's November meeting programme
- contributes to organisation of scientific sessions at BES meetings

Publications Committee
(Chair: John Wass (General Secretary), Oxford)
- ensures that Society's journals meet the agreed academic and production standards
- advises Council on journal budgets and prices
- makes recommendations to Council on the selection of Editors

Science Committee
(Chair: Barry Brown, Sheffield)
- provides input on scientific sessions at the November and BES meetings
- helps to define the professional training of scientists
- presents the Society's views on professional and policy issues to Government and other bodies
- oversees the programme for the Molecular Endocrinology Workshop at Summer School

All committees meet at least twice annually, and report to the Council of Management which consists of the four Officers and eight Trustees who are formally elected at the AGM. New committee members are elected from nominations made by members, which are requested via *The Endocrinologist* and the web site.

COMMITTEE NEWS - *The latest from each of the Society's committees.*

AWARDS As well as selecting a clinical fellowship funded by the Clinical Endocrinology Trust/Society for Endocrinology, this committee is currently considering the nominations you have made for awards at BES 2006 and November 2005.

BES All the scientific sessions for BES 2005 have been finalised, the Harrogate venue is booked and all speakers have been invited. Importantly, the ever-popular social and sporting events have also been confirmed.

CLINICAL Sessions are being developed for submission to the organising committees for November 2005 and ECE 2006. In addition, this committee has compiled the Society's statement on the use of testosterone.

FINANCE The annual management accounts and financial statements show excellent results. The surplus on activities will help repay the cost of new premises, and last year's loss on investments has been reversed. Ways of presenting the accounts more accessibly have been discussed. The parameters for reviewing our stockbrokers have also been agreed.

NURSE Programmes for the 2005 training course and sessions at November 2005 and BES 2006 are in development. Three Certificates in Adult Endocrine Nursing have now been awarded, and several more nurses are currently completing the qualification.

PROGRAMME The abstracts for November 2004 have been marked by a panel of independent markers and grouped in preparation for the meeting. The committee will meet at the November meeting to begin planning the November 2005 meeting.

PUBLICATIONS Open Access and its implications for the Society's publishing activities are on the agenda (see article on page 8. Meanwhile, the strength of our publishing is reflected in ever-increasing journal impact factors (see page 3). Various editorial and pricing strategies have been discussed, to ensure this trend continues.

SCIENCE As well as making programme suggestions for November 2005 and BES 2006, this committee has developed a postgraduate diploma for scientists in endocrinology. Eight candidates have already registered since its launch at BES 2004.

Council last met in September and an update will be included in the next issue.

Nominations needed now!

Send nominations to fill vacancies on the Awards, Clinical and Science Committees to Chris Davis in the Bristol office by 19 November 2004. Nomination forms are available at www.endocrinology.org/sfe/commit.htm or from christine.davis@endocrinology.org. For information about opportunities to join other Society committees email info@endocrinology.org.

Review lecture

Congratulations to Dr Karen Piper, the Society's Young Endocrinologist Basic Science Review Lecturer for 2004. She will present her lecture, 'Understanding endocrine development of the human beta cell: guiding stem cell therapy for type 1 diabetes', during this year's November meeting (see advert on page 12 for further event details).

Top honours

Professor Paul Stewart, from Queen Elizabeth Hospital in Birmingham, is to deliver the Endocrine Society's 2005 Clinical Investigator Award Lecture. This is a major honour, particularly for a European endocrinologist. This is in addition to his recent Graham Bull Prize from the Royal College of Physicians, the major award for clinical research by a UK clinical scientist under 45. We offer Paul our congratulations.

Strategic review 2004-2009

Council's recent review of the Society's strategy examined objectives set in 1998-1999, and brought them into line with current requirements. It has also provided a 5-year business plan, taking financial implications into account. Council approved the review earlier this year, and the revised strategy came into effect from May 2004 (the beginning of the current budgetary year).

The Society's overall objective of advancing public education in endocrinology is unchanged and is our charitable object. The five existing aims have been slightly updated:

- to advance education and research in endocrinology for the public benefit
- to be the voice of endocrinology in the UK
- to be a major focus of endocrinology outside the USA
- to support endocrinologists worldwide and to foster a sense of community
- to raise the profile of endocrinology

Financially, the Society's healthy position has resulted from adjustments to our spending plans that were made 3 years ago in the light of stock market losses. Our overall aim is to spend our income and break even once our reserves hit new targets. Because we generally budget cautiously, we usually perform better than budgeted. Any surpluses are used to build our reserves, if these are lower than the level specified by our reserves policy. (Recent capital expenditure on the new offices means that this is currently the case.) Once the reserves are sufficient, surpluses are spent in the following year. One key decision is that studentships and fellowships should only be funded when finances allow. This has meant that no new grants have been made in the last few years, but the programme is gradually being reinstated, starting with the Clinical Fellowship, funded jointly by the Society and the Clinical Endocrinology Trust.

As the range of clinical and scientific endocrinology is so broad, it has been agreed that key areas should be selected and developed proactively. Topics were chosen that are poorly covered at main meetings; they are diabetes, oncology, cell biology, and bone and mineral metabolism.

Having considered the overall strategy, Council has made plans for the next 5 years. In this first year, main areas for action will be:

- setting up the first four Special Interest Groups (PCOS and the metabolic syndrome, pituitary, steroids, bone and mineral)
- reviewing the Society's committees, to be undertaken by a working group led by John Wass
- reviewing the Society's meetings, particularly in the light of plans for an annual European Congress of Endocrinology. Ann Logan will lead this working group.

The full strategic review is available at www.endocrinology.org/sfe/stratreview0409.htm (same password as for handbook), or contact rachel.evans@endocrinology.org for more information.

2005
SUMMER SCHOOL

5-8 July 2005
ST AIDAN'S COLLEGE, DURHAM

5 July
Molecular Endocrinology Workshop

6-7 July
Advanced Endocrine Course

8 July
Clinical Practice Day

Grants are available for younger Society members to attend the workshop.
See www.endocrinology.org/sfe/grants.htm for further details.
Deadline for grant applications: **15 April 2005**

OBITUARY

Jean Ginsburg

Dr Jean Ginsburg, formerly a Consultant Endocrinologist at London's Royal Free Hospital, died on 8 April 2004, aged 77. She was born in London in 1926, the daughter of Jewish political refugees from revolutionary Russia.

Jean won a scholarship from St Paul's School to Somerville College, Oxford, to read medicine, and became one of the first women to qualify from St Mary's Hospital, Paddington. Her research career began at St Thomas's Hospital, where she used forearm venous occlusion plethysmography, then a new means of measuring blood flow in the limbs, to study circulatory changes during pregnancy and the menopause. In 1966, when scientific reproductive endocrinology was in its infancy, she moved to the newly established department of Obstetrics and Gynaecology at the Royal Free Hospital, where she helped set up a gynaecological endocrine service.

It was very much to her credit, and typical of her attitude to women's healthcare, that she established one of the first UK clinics for the menopause when part of the Royal Free Hospital was located at New End. At this time, there was relatively little therapy available for the climacteric. She demonstrated clearly, using simple circulatory techniques, that the menopausal hot flush was essentially a reflex phenomenon, not an emotional reaction, and that it reflected a disturbance of thermoregulatory mechanisms.

In the late 1960s and early 1970s, when urinary gonadotrophins became available for use in female reproductive disorders, she established the first ovulation induction programme. This interest continued until the time of her retirement. She published over 250 peer-reviewed articles and edited several books, including *Drug therapy in reproductive endocrinology*.

Jean was fiercely individualistic and had an insatiable appetite for work. It is said that one 'experienced her' rather than 'knew her'. Colleagues were often struck by her incisive intelligence but equally, on occasions, her idiosyncratic views and endocrine practice. Whilst these sometimes conflicted with mainstream endocrinology, there was little doubt of her commitment to her patients and her belief in holistic practices.

Fluent in both Russian and French, Jean was well read. She was also an accomplished pianist, with many interests outside medicine, including opera and fine wines, the benefits of which she never ceased to advocate. She will be remembered best, however, for her work, which put her at the forefront of the use of gonadotrophins in female reproductive disorders.

She is survived by her husband and their daughter, two sons and three granddaughters.

PIERRE BOULOUX AND GORDANA PREVELIC

With regret

We are sorry to announce the death of Professor G E Lamming on 24 June 2004. An obituary will follow.

Endocrine nurse news

The 2nd International Congress of Endocrine Nursing (ICEN) entitled 'Global Endocrine Nurse Issues: Their Commonality and Diversity' was held in Lisbon last month. It was organised primarily by three nurses: Maggie Carson (representing SfE), and two Americans: Molly Solares (ENS) and Diane Lee-Smith (PENS), with input from the Australian Endocrine Nurses Society (AENS) led by Bin Moore.

Of the 53 nurse delegates from nine countries (Australia, Canada, Ireland, The Netherlands, Portugal, Sweden, Switzerland, UK and USA), five were from the UK. The meeting lasted three days and was made up of four half-day sessions, each organised by PENS, ENS, AENS and SfE EN. In addition, there was a cocktail reception and a poster exhibition. The sessions were all well attended and promoted lively discussion and debate. It was interesting to discover how widely practices vary across the globe e.g. in Australia growth hormone replacement is still only available to children.

It was also interesting to note that, of all the countries represented at ICEN, we are the only one to have established an annual endocrine nurse training course and to have a recognised Certificate in Endocrine Nursing. An Australian nurse attended our 2004 training course in Bristol last month and the Swedish (12) and Dutch (2) nurses in Lisbon hope to attend future courses.

Planning will soon be underway for the 3rd ICEN in Rio de Janeiro in 2008.

MAGGIE CARSON

Members on the move...

K Ahmed to West Middlesex University Hospital, Isleworth; E Anderson to AstraZeneca plc, Macclesfield; A Baird to University of Birmingham; J Dale to Wordsley Hospital, Stourbridge; R Fowkes to Royal Veterinary College, London; A M Gonzalez to University of Birmingham; C Harvey to Royal Free Hospital, London; G Rumsby to UCL Hospitals, London; T Siebler to Hôpital Kirchberg, Luxembourg; A V G Taylor to Shoalhaven Memorial Hospital, Nowra, Australia; F Wotherspoon to Derriford Hospital, Plymouth.

L to R: Suzanne Curran (Cambridge), Kate Davies (London) and Maggie Carson (Edinburgh) at ICEN

Webspinning

Melissa Westwood highlights the best on the web

(Gene) silence is golden

www.orbigen.com/commerce/misc/techwatch.jsp

RNA interference, or RNAi, is the most exciting recent technology for controlling eukaryotic gene expression. This web site, which is updated daily, does a noteworthy job of covering this rapidly evolving topic by providing links to relevant publications, informative PDF files and prominent labs in the field. A rare one-page summary of an important subject! SERVICES: L, O (PDF links); STRONG POINTS: Research information; WEAK POINTS: Could be better organised; RATING: Good.

Clone forth and multiply

www.reproductivecloning.net

The wide public discussions arising from the cloning of Dolly the sheep look to be superceded by the controversy surrounding human cloning. So what better time for a resource like the Reproductive Cloning Network? The site aims to provide fundamental information on the science underlying reproductive cloning and also to store, link to and review scientific resources regarding the subject. It certainly makes for some interesting reading. SERVICES: L, N, O (message board); STRONG POINTS: Good design; WEAK POINTS: Editorial bias; RATING: Very good.

A fan-stat-ic web site

socr.stat.ucla.edu

Hosted by UCLA, this site provides a large collection of Java applets for online analysis of data by various statistical techniques. As the site is primarily aimed at students, instruction manuals, demonstrations and tutorials in the form of interactive computer games also feature highly. My guess is that it's not only students that will benefit from these! SERVICES: S, L; STRONG POINTS: Online/downloadable tools; WEAK POINTS: None; RATING: Very good.

Thanks to Kevin Ahern and *Genetic Engineering News*. Don't forget to visit the Society for Endocrinology on the web: www.endocrinology.org; tell us about your favourite web site: melissa.westwood@man.ac.uk.

KEY **Services** provided at web sites:

- **T** Tools - Analytical computing tools
- **D** Data - Searchable or downloadable database information
- **G** Goods - FTP delivery of useful items (e.g. full package, bug fix or demo software)
- **L** Links - Useful links to other sites
- **N** News - News of interest
- **S** Support - Feedback in response to users' enquiries
- **O** Others - e.g. Innovative use of web tools, appearance, editorial point of view

Ratings: Excellent, Very Good, Good

Nothing below good will be reported here.

Be the best at BES!

It's that time of year again - time to prepare your submissions for the next BES meeting. And what greater incentive than the prospect of winning one of the coveted awards at the meeting? Our thanks go once again to the sponsors of these prizes. **Remember that your abstracts must be submitted by 12 November!**

BES Awards supported by Pfizer Ltd This is the eleventh in a series of awards for clinical and basic science laboratory research proposals in the field of endocrine growth factors. The successful proposal will receive the major award of £10 000, and five additional travel grants of £500 will also be available. The judging panel comprises members appointed by the Society for Endocrinology Awards Committee and a Pfizer Ltd nominee. All applications must be for research carried out within the UK or Ireland. Please contact Feona Horrex at the Bristol office for an application form (Email: conferences@endocrinology.org), which must be returned by 10 January 2005.

Novartis Awards Two prizes of £1000 are offered by Novartis Pharmaceuticals UK Ltd for the best abstract submissions by young endocrinologists. The first author must be less than 35 and no further than 6 years post PhD/MD/MRCP. Please indicate on the abstract form if you would like to be considered for one of these awards, so that the Programme Organising Committee can consider your abstract for nomination.

British Thyroid Association Award This award of £500 will be made to a young researcher who submits a high-scoring abstract of relevance to the thyroid. The first author should be under the age of 35, and must submit their abstract in the 'thyroid' category.

Society statement on the use of testosterone

The Society has formulated a statement which can be found at http://www.endocrinology.org/SFE/briefings.htm

Bioscience and business: commercialising your research

The Biosciences Federation is holding a one-day symposium 'Bioscience and business: commercialising your research' on Tuesday 12th October 2004 at the Royal Society, London. World-class speakers will discuss some of the practical issues surrounding the commercialisation of bioscience, such as how to attract investment, developing partnerships with industry and intellectual property arrangements. Society for Endocrinology members can attend at a reduced rate. For more information and a booking form call the Conference and Events Manager on 020 7581 8333.

Open Access: should journals be free for all?

Steve Byford examines the issues and asks what would a change to open access mean for science and the Society

Scholarly literature should be available freely online, with no access restrictions. There's been an increasing amount of talk about this idea, usually called Open Access, both in the general press and in the scientific literature. Open Access journals would be funded instead by charges to authors - or rather their funding bodies. The Society has been considering it carefully for some time, and it continues to be a hot topic.

A recent related development is the Open Archive Initiative, which encourages institutions to set up online repositories for their researchers' papers, which would then be available freely to all. This might not seem an immediate threat to traditional journals, as no one wants to search across many institutions' web sites. However, new developments would allow readers to search across many such repositories from special centralised search engines. Why should libraries pay for journal subscriptions if their readers can easily access the same papers for free?

Open Access journals have been with us for some time, notably from BioMedCentral, a commercial company, which has charged authors $500 (whilst estimating that its costs are probably four times this). Lately the Public Library of Science (PLoS), originally a pressure group, has become an Open Access publisher, with *PLoS Biology* and *PLoS Medicine* already launched, and more titles promised. PLoS charges $1500 per article but admits that this does not cover its costs.

There was recently a bill before the US House of Representatives (the 'Sabo bill') that said 'publicly funded research should be publicly available'. The implication was that the funding for research would cover the costs of publication, but this was not stated explicitly. Perhaps there was a naïve assumption that there would be no costs. Several US newspapers picked up the story and ran articles criticising publishers' outrageous profits, the apparent implication being that all scholarly publishers were equally guilty. Pressure from librarians is also continuing - it is often attributed to the academics they serve, but we've rarely heard from endocrinologists who are passionate about this!

More recently still, the UK House of Commons Select Committee on Science and Technology (to which the Society made a submission) has produced a report including, amongst its 82 conclusions, a recommendation that all UK-funded research output be deposited on free online institutional repositories. In the US, the NIH has produced draft proposals that would require all NIH-funded authors to place their final, accepted manuscript on PubMed Central for free access, and for journals publishing the papers to make them freely available no more than six months after publication. The publisher Springer has announced an optional author-pays, free-to-reader scheme ('open choice') for its journals. Elsevier now permits authors to deposit their accepted papers on free-to-reader institutional repositories.

What should the Society's view be?

What's wrong with the current system?

It's sometimes argued that the subscription model has served the academic community well for decades, producing high-profile quality-assured journals. Why throw that away? Wouldn't it be better to defend it vigorously? The trouble is that it has some deep flaws, leading some to wonder how long it can remain viable.

Perhaps the strongest symptom is the fact that most mature journals lose a small percentage of their library subscribers every year. Since most of the costs of publishing are independent of the number of copies produced, publishers' unit costs increase, which forces up journal prices. This leads to a vicious cycle of further cancellations, since library budgets can't keep up. The underlying cause is not primarily irresponsible pricing by publishers (although not all have been entirely innocent), but the mismatch between the funding for research on the one hand, and the funding for the dissemination of its results on the other. Over the last several decades, the amount of scientific research being done around the world has grown enormously, resulting in more and more research papers, which needed to be published in more or bigger journals. Libraries have not usually been provided with anything like the same proportion of extra money with which to buy them. So the round of cancellations began.

That's not the only problem. The journals market is dysfunctional in other ways. For example, if you were to sit down and compare the prices of journals with their perceived quality, or with their impact factor ranking, you might be in for a shock. We have come across journals from large commercial publishers with prices up to five times that of higher-impact, comparably sized direct competitors from not-for-profit learned societies. Why haven't market forces corrected this? It's perhaps largely because of the fact that the decision to publish in a particular journal is divorced from financial factors - librarians know all about prices, and researchers know all about quality ranking. The two issues get pondered in two separate sets of heads.

Are there other solutions?

Against a backdrop of restricted purchasing power by libraries, how might the Society seek to disseminate its journals more widely, and still protect its subscription revenue? It's a good question, because we've historically relied on our journals to be a major contributor to funding all the other things we do for the benefit of endocrinology, in fulfilment of our charitable remit. This remains largely the case, even though we've succeeded in developing other revenue streams, via BioScientifica's growing range of services.

One approach is to find ways of giving a lot more online access (which doesn't cost much to provide) to additional sites that wouldn't have been able to buy additional conventional subscriptions, and to do so for a comparatively small amount of extra money. This is something that appeals to consortia of universities, for example, only some of whose members currently have an institutional subscription, or to large companies who want online access to their entire corporate network across many sites. Clients get wider access, we get wider dissemination and a little more money - everyone wins!

Well, almost. The trouble is, setting up and maintaining the terms of these deals is a labour-intensive process. Librarians also find it easier to justify their time if they can negotiate for a large number of journals at once, meaning that the large commercial publishers end up with a considerable advantage, not least because they find it easier to send out large, region-specific sales forces. Librarians often end up committing large proportions of their budgets, often over several years, to the very publishers they say over-price for lower-quality journals, whilst squeezing the amount that's left for the smaller publishers whose products they say offer better value. It's an odd world.

The Society has tried to combat this by co-operating with other small not-for-profit publishers to offer its journals jointly with theirs. For example, we've recently signed up to one initiative that offers 430 journals from 44 diverse international small publishers. That should make us a bit more noticeable.

However, whilst 'multi-site licencing' stands a good chance of alleviating the symptoms of the current problems, it doesn't really address their root cause. It also needs a lot of administrative effort.

How could Open Access help?

Immediate freedom of access to scholarly research results is intuitively attractive to us all. As readers, we want ease of access from any location, as authors we want our work to be disseminated as widely as possible. These expectations are frustrated by a system that restricts access to just those journals our own library can afford.

The mismatch between funding for research and for its dissemination could be removed at a stroke if research funding bodies included, as part of their research grants, funds for authors to pay for the publication of their results.

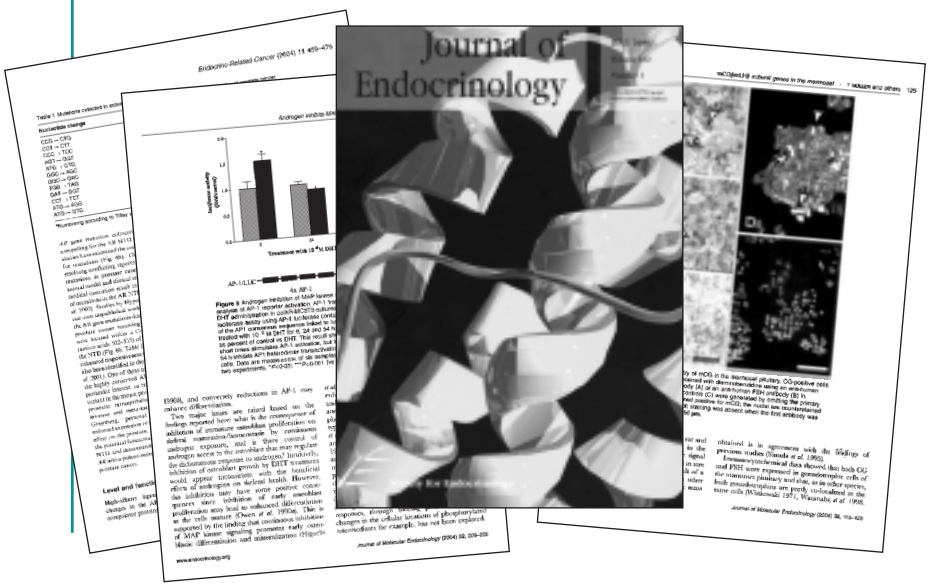
The current mismatch between the price and quality of journals would be directly under attack if an author's choice of journal were influenced not only by the journal's perceived prestige and quality but also by the publication costs. Any price differentials would then be transparent to the researcher and the market would force a link between price and quality.

Under the new model, publishers would sell a service to authors. They would be judged by the extent to which they maximised the exposure and credibility of the work they published, and by how much added value they gave the work compared with authors merely depositing their manuscripts on their institutions' online repositories.

The Society has been enthusiastic about the principle of an Open Access model for some time. As far back as 1999 we were suggesting that the research grant, rather than the library budget, would be a better funding route for research dissemination, for precisely the reasons outlined above.

Why delay? Open Access today!

Well then, what's to stop us embracing the new model? It's perhaps obvious that it won't work for every kind of journal: what about clinical research for which there is no grant? Similarly, it's difficult to see how review journals could be financed this way. Even so, what's to stop us switching our basic science research journals over to Open Access? How do we make the transition?



There's the rub. A promising route that captured the Society's imagination was the so-called 'hybrid transition model'. Charge the authors an optional fee: if they choose to pay, their article becomes free to all; if not, it's restricted to subscribers, as at present. That looked as though it might take us forward while limiting the risks.

Until you project the money we might get. Our financial viability then turns out to depend precariously on a few key parameters. Firstly, how much should we charge authors? Then, what proportion of authors would take it up? Finally, how would this affect our subscription income? The answer to the first affects the second, which in turn affects the third. Set the price too low and we won't get enough money to cover our costs, and we encourage a high level of take up. If that means a substantial fraction of the journal is free, many librarians will heave a sigh of relief and cancel their subscription. Under certain very plausible scenarios, that could kill the journal that tries it. Set the author fee at a more realistic level and it will be perceived as extortionate, and we lose the sympathy and loyalty of our authors and readers.

It's quite scary. Tweak these parameters by not a lot, and the Society could either be rolling in extra cash or, quite simply, permanently out of business. Worse still, because the effects on subscriptions would not be immediate, it could be two or three years before a fatal decision took its toll - we wouldn't know until then what its effect had been.

And that's frustrating. We have here a new model that could solve everything, but which could destroy everything as we edge towards it. It's as though an Open Access paradise is visible to us in the distance, but in order to get there we have to cross a bottomless ravine using an unsafe rope bridge.

Unless we can find another way over. Can we launch an Open Access experiment without serious risk to our financial viability? This is exercising our minds greatly at the moment. Meanwhile, your Council and Publications Committee would be extremely interested to hear your views! And then, as they say, watch this space…

Comments, please, to Steve Byford at the Society's office or via the website at www.endocrinology.org/sfe/forms/contactform.htm.

NET effects

Martyn Caplin takes a closer look at neuroendocrine tumours of the gastroenteral tract and pancreas.

Neuroendocrine tumours (NETs), derived from the diffuse endocrine system, can be found anywhere in the body. Most common are carcinoid tumours (derived from foregut, midgut and hindgut), pancreatic islet cell tumours (mainly insulinoma, gastrinoma, vasoactive intestinal polypeptide (VIP)oma, glucagonoma and non-functioning tumours), pituitary tumours, phaeochromocytomas, paragangliomas and medullary thyroid cancer. This review concentrates on gastroenteropancreatic (GEP) NETs.

GEP NETs are relatively rare (e.g. carcinoid tumours: 2.5-4.5/100 000 population per year in the USA; pancreatic NETs: 5-10/million population per year), but in the past 20 years the incidence has almost doubled. However, they are usually slow-growing, with a prevalence much greater than their incidence: Postmortem studies suggest at least 1% of the population have a NET, reflecting their indolent nature. Symptoms may be non-specific, although some patients live a relatively normal life for many years despite metastatic NET. In others the tumour will run a more aggressive course. Poor prognosis appears to be related to increases in tumour size, poor size differentiation, high proliferative index (Ki67) and metastasis to other organs such as bone and liver. However, the median time to diagnosis can be 3-7 years.

The heterogeneous group of NETs were once all classified as one biological phenotype, misrepresenting their biological and behavioural diversity. The latest WHO classification gives a more informed description and diagnosis, classifying tumours by site of origin, functional or non-functional nature, pathological activity and differentiation. This results in subclassification into: (a) well-differentiated endocrine tumours with either benign behaviour or uncertain benign or low-grade malignant potential; or (b) poorly differentiated endocrine cancers with high-grade malignant behaviour. Microscopically, NETs are trabecular, glandular or form rosettes. The tumour cells are similar in appearance, with faint pink granular cytoplasm, round nuclei and usually with few mitoses. Their histological diagnosis relies on immunohistochemistry, first to identify general markers of neuroendocrine differentiation (using antibodies against secretory granule proteins (chromogranin A (CgA), synaptophysin) and cytosolic proteins (neurone-specific enolase, protein gene product 9.5), and then for cell-specific characterisation.

Carcinoid tumours derive predominantly from enterochromaffin or Kulchitsky cells; they are subdivided according to embryological origin as foregut (bronchus, stomach, pancreas), midgut (small bowel, appendix and caecum) and hindgut (colon, rectum). The more aggressive include the sporadic type III gastric carcinoids, duodenal carcinoids >2 cm, midgut carcinoids (which often present with the carcinoid syndrome, having metastasised to the liver), and more invasive rectal carcinoids. Colonic carcinoids often have the worst prognosis and present with metastatic disease. Fewer than 10% of patients complain of the carcinoid syndrome, which includes flushing, diarrhoea, wheezing, abdominal pain, heart disease and pellagra. The ability to synthesise 5-hydroxytryptamine (serotonin) from dietary tryptophan is pathognomonic. Subsequent production of 5-hydroxyindoleacetic acid (5-HIAA) is classically associated with carcinoid tumours, but urinary 5-HIAA has high sensitivity only in midgut carcinoid. Many other hormone products of the tumour cells (kinins, prostaglandins, substance P, somatostatin, corticotrophin) cause signs or symptoms only if released directly into the systemic circulation; CgA in plasma, however, is a sensitive marker for all types of carcinoid tumour.

Features of pancreatic NETs are summarised below. Their biochemical diagnosis includes measurement of both the appropriate peptide and plasma CgA, which usually increases with tumour burden. At presentation, 50-90% of pancreatic NETs have metastasised; however only 10% of insulinomas metastasise.

Multiple endocrine neoplasia type 1 (MEN-1) occurs in 20-40% of gastinomas and non-functional pancreatic NETs but less than 5% of insulinomas and carcinoid tumours. The mutation has been identified on chromosome II and the syndrome characterised by primary hyperparathyroidism, tumours of the endocrine pancreas and anterior pituitary. Other hereditary neoplasia syndromes associated with NETs included neurofibromatosis type 1 and von Hippel-Lindau disease.

Robust imaging is required for the management of GEP NETs for most NETs possess somatostatin receptors, with type 2 predominating, the most sensitive modality is somatostatin receptor scintigraphy (OctreoScan). In diagnosis, sensitivity is 50-80% for primary tumours and ~90% for metastatic tumour. The addition of single photon emission tomography should be

Tumour	Location	Symptoms	Diagnostic tests
Insulinoma	Pancreas	Confusion, sweating, dizziness, weakness, unconsciousness, relief with eating	Fasting insulin, glucose, C peptide, (sulphonylurea screen negative)
Gastrinoma	Duodenum 50% Pancreas 50%	Zollinger-Ellison syndrome	Fasting gastrin, gastric acid secretion
Glucagonoma	Pancreas	Diabetes mellitus, necrolytic migratory erythema, weight loss, confusion, diarrhoea	Plasma glucagons, glucose
VIPoma	Pancreas 90% Extrapancreatic 10%	Werner-Morrison syndrome	VIP and pancreatic polypeptide
Somatostatinoma	Pancreas 55% Duodenum 45%	Cholelithiasis, weight loss, diarrhoea and steatorrhoea. Diabetes	Plasma somatostatin
Non-functional pancreatic NET	Pancreas	Symptoms from pancreatic mass and/or liver metastases	Plasma pancreatic polypeptide, ±HCG, calcitonin

routine, increasing sensitivity by 25%; hybrid fusion with computed tomography (CT) also increases sensitivity. I-123 mIBG imaging has a sensitivity overall of 50% for carcinoid and just 9% for pancreatic NETs. After improvements in technology, the sensitivities of spiral CT and magnetic resonance imaging for detecting primary disease are now ~50-70%. For both modalities, overall sensitivity for metastatic disease is ~80-90%.

Ultrasound has a low sensitivity for detecting the primary tumour, but is useful for detecting metastatic disease, and intraoperative ultrasound is a highly sensitive tool, especially as often more than one tumour may be present at the time of surgery. Endoscopic ultrasound has the highest sensitivity (>90%) for detecting pancreatic NETs and determining invasion of gastric and rectal carcinoids. Angiography and visceral sampling may be useful in detecting small pancreatic NETs, especially insulinomas.

The aim of therapy is to manage patients according to the biology of their tumour. There are several approaches. Somatostatin is a hormone that inhibits the release of peptides associated with endocrine syndromes. It has a short half-life (2-3 min), so synthetic analogues (octreotide, lanreotide and others) were developed. They are effective in controlling NET hormonal syndromes, reducing flushing and diarrhoea of carcinoid syndrome in 60-70% of patients.

Octreotide is usually given as a subcutaneous injection in doses of from 50µg twice daily to 500µg three times daily. It can also be given intravenously. In cases of carcinoid crisis (usually precipitated by an anaesthetic or interventional procedure in patients with carcinoid tumour), treatment is a bolus intravenous injection of 100-500µg octreotide, continued if necessary as 50µg/h infusion for a further 24-48h (intravenous antihistamine and hydrocortisone may provide additional benefit). Longer-acting agents include a once-monthly intramuscular preparation, Sandostatin LAR (standard dose usually 20-30mg per month), and Somatulin LA (30mg every 2 weeks intramuscularly) which is being replaced by lanreotide autogel (deep subcutaneous injection of 60-120mg every 28 days). Efficacy appears to be similar between agents. Adverse effects (pain at injection site, abdominal cramping discomfort and diarrhoea) may occur, but rarely cause discontinuation of treatment. Gallstones may develop in up to 60% of patients receiving long-term treatment.

Surgery is the only chance of cure. Patients often have metastatic disease at presentation, and the practice of removal of primary tumour and subsequent resection of liver metastases has developed recently. Debulking also appears useful, benefitting survival and enhancing the response to other therapies because of diminished tumour burden. Surgical management depends on tumour site, mass effect, invasion, size, biology and metastases. Orthotopic liver transplantation is associated with a high risk of recurrence. Patients should be considered only if there has been robust exclusion of extrahepatic disease and if the tumour is low-grade.

Interferon α (IFNα) inhibits the cell cycle and production of growth factors and receptors secreted by the tumours, and has an antiangiogenic effect and an immunomodulatory effect by stimulation of natural killer cells, macrophages. The biochemical response rate in NETs is about 50% and reported objective response rates are 0-30%. Combinations of IFNα and somatostatin analogues have given variable results, but may be associated with some tumour stability. Interferon therapy seems best suited to patients with tumours of low proliferative index and small volume disease.

There has been little advance in chemotherapy since the 1980s, and no role exists for single agent chemotherapy. However, chemotherapy may be considered for advanced progressive foregut tumours, which are chemosensitive. A combination of streptozocin and 5-fluorouracil, with or without adriamycin, or combinations of agents such as etoposide, lomustine and dacarbazine, significantly prolongs survival, with evidence of objective response in 40-60% of patients with these tumours. Patients with poorly differentiated tumours have an objective response of 60% to cisplatin regimens, but suffer from early relapse. Typical midgut and hindgut carcinoids have a poor response to chemotherapy combinations (<30%).

Hepatic artery embolisation is an effective ablation treatment for hepatic metastases, reducing hormonal symptoms and tumour burden and increasing median survival. Objective response rates may be further improved by combining embolisation with cytotoxic agents, but there are no controlled trials suggesting that chemoembolisation is any better than particle embolisation alone. Embolisation should be used with caution when more than 75% of the liver parenchyma is replaced by tumour. Patients with carcinoid syndrome need octreotide continued for 24-48h post procedure.

Radiofrequency ablation, a novel method for destroying liver tumours by selective thermocoagulation, may be performed percutaneously or at laparotomy or laparoscopy. Initial results suggest benefit in objective response and reduction in hormone secretion. Consideration of this therapy must take into account number of lesions, site (distance from vessels), and benefits compared with surgery, embolisation or radionuclide therapy.

Radionuclide therapy, like imaging, is based on the ability of NETs, to avidly take up indium-111-octreotide or [^{123}I]MIBG for scintigraphic scanning. The tumour is initially visualised with the diagnostic scan that enables an estimate of tumour load. Then the isotope label on the peptide is changed, preferably for a β-emitter, to target the radiotherapy to the tumour cell. [^{131}I]MIBG therapy is the only radionuclide therapy licensed for NETs and has clinical activity (biochemical response) in up to 70% of patients treated, with objective response ~25%. ^{90}Y-DOTA octreotide is not currently widely available and whilst the majority of patients achieve tumour stabilisation, significant tumour regression is seen in only about 20% of patients. With ^{90}Y-DOTA lanreotide, 41% achieved stable disease and 14% achieved regression. Lutetium-177-DOTA octreotide is now available and appears to be particularly good for targeting small-size diffuse metastases. All agents based on somatostatin analogues are currently considered experimental. Toxic effects of radionuclide therapy include myelosuppression, particularly lymphopaenia, and nephrotoxicity. Pretreatment with amino acids, particularly D-lysine, reduces renal tubular octreotide binding and minimises renal damage.

Little evidence-based guidance exists for the management of NETs, and controlled trials are needed to establish best practice. Patients present to a variety of medical and surgical specialties, thus their management within the context of a multidisciplinary team is imperative, and appropriate patients must be carefully selected for therapy, considering both the effect of treatment on patient survival and their quality of life. To optimise their care and recruitment to appropriate trials, NET patients should be seen only in centres with a specialist interest. The UK NETwork group (uk-network.org.uk) aims to co-ordinate clinical and scientific collaborative studies, promote education including an annual conference (15 November 2004), and produce guidelines planned for publication early in 2005.

MARTYN CAPLIN

The rise of aromatase inhibitors

Anthony Howell discusses advancements in breast cancer therapy that could see the end of 'the hegemony of tamoxifen'.

Endocrine therapy has been an important treatment for breast cancer for over 100 years. Tumour growth is inhibited in patients with oestrogen receptor (ER)-positive tumours, either by blocking the ERs using anti-oestrogens or by reducing oestrogen concentrations in the peritumoural environment.

The anti-oestrogen of choice for many years has been tamoxifen. It has been shown to be effective in reducing the tumour burden in advanced breast cancer, increasing survival when used after surgery for primary disease, and reducing tumour incidence by about 40% in women at increased risk of breast cancer. However, the hegemony of tamoxifen is now being challenged by modern aromatase inhibitors (AIs). Their relative lack of toxicity and ease of administration (daily tablets) has led to wide assessment of their use in breast cancer.

AIs inhibit the aromatase enzyme reversibly (anastrozole and letrozole) or irreversibly (exemestane), resulting in barely detectable levels of oestradiol in peripheral blood. They are superior to megestrol acetate as second line treatment, and to tamoxifen as first line treatment for advanced breast cancer. More recently, a large series of trials was established to compare each AI with tamoxifen as adjuvant therapy.

To date, these studies indicate that, when treatment is initiated soon after surgery, 5 years of treatment with anastrozole is significantly superior in preventing relapse to 5 years of tamoxifen. Two trials (one with anastrozole and the other with exemestane) demonstrated a reduction in relapse if tamoxifen was switched to an AI after 2-3 years of treatment, rather than continuing with tamoxifen for 5 years. In addition, starting an AI (letrozole) after completion of 5 years of tamoxifen is more effective than giving no further treatment. In all of the tamoxifen versus AI adjuvant trials, contralateral breast cancer (CBC) is reduced by about 40%.

These findings are in addition to the known preventative effect of tamoxifen on CBC incidence, and have led to the inception of two large breast cancer prevention trials in high-risk women. Anastrozole is being compared with placebo in one study (IBIS II) and exemestane with or without a cox-2 inhibitor versus placebo in another, North American, programme.

The prevention trials began partly because of the increased efficacy of AI on CBC, but also because of their better tolerability profile compared with tamoxifen. AIs are associated with fewer thromboembolic and gynaecological events (they may actually prevent endometrial cancer), but at the expense of the induction of joint aches in some patients and an increased fracture rate. Studies to determine how to prevent bone loss in the low oestrogen environment induced by AIs have shown promising early results. For example, a group in Austria has demonstrated that 6-monthly 15-minute infusions of 4mg zoledronic acid could prevent the bone density reduction seen when premenopausal women are treated with a combination of goserelin and anastrozole. It will also be important to ensure that the low oestrogen environment has no deleterious effect on cognitive function. A subprotocol of the IBIS II trial should help, since cognitive function will be measured in 700 of the 6000 women anticipated to enter the trial.

In conclusion, AIs are becoming the treatment of choice when compared with tamoxifen for the treatment of early and advanced breast cancer. How much better they will be, and whether one AI will prove to be superior to others, awaits the long-term results of the trials underway.

ANTHONY HOWELL

A 'personal best' for endocrinology?

Just a few weeks ago, I was invited to speak at a runners' reception one evening. Its purpose was to thank the 80 members of the public who had run in the London Marathon, the Great North Run and the Manchester 10K, thereby raising between £50 000 and £100 000 dedicated to the hospital. I guess I was chosen to speak because our unit has an active research programme that has often benefited from such sponsorship in the past. Furthermore, although not a runner by body design or nature, I happened to have run a few half-marathons and also the Manchester 10K. In other words I was both a research fund recipient and a fellow-sufferer.

It was interesting to consider, for a non-runner like myself, how little one is prepared for the suffering that lies ahead. 'Drink plenty of fluids on the day of the race,' they say. But no-one warns you about the length of the queue for the toilets. Better to be fitted with a catheter: innovative sponsors please note! Then there are runners' nipple and groin irritation, both of which could have been avoided if you had been told about Vaseline. Finally there's the mental suffering; having crawled past the finish and been given your medal, another man appears and stuffs a leaflet in your hand, informing you that the next half-marathon in your region is the following week. Your only reply, if you have the breath to ask it, is in the form of a question, 'How many hospitals lie on the route?'

Beyond the suffering is the mental humiliation. I ran one local half-marathon in which, as well as a number on our back, we had a letter to indicate our 5-year age bracket. Mine was G, which covered the range 45-50 years, and to my horror at 10 miles I was overtaken by a small woman with T on her back. Even worse, whilst running in the Manchester 10K this year, I was passed by a banana in pyjamas - and fairly tasteless pyjamas at that!

Such races also provide a sense of perspective. In the Wilmslow half-marathon, I came 1200th out of 2000 runners, but my time was good enough to place me third in the over-eighties female category. I have never looked at myself in the mirror in the same way again.

It is that sense of perspective that allowed me to appreciate not just the scale of the research funding that had been raised for the hospital by these runners, but also what heroes lie in amongst a group of individuals that might superficially be considered an ordinary community. The runners included some patients in the middle of their cancer treatment, but most individuals ran out of love for those surviving serious disease, or in memory of those that hadn't. Teenagers, pensioners, people with disabilities, and some who raced in chairs were all in the audience.

It was a truly humbling experience to meet and talk to them, but I felt a sense of inadequacy in being unable to match their achievements, dedication and giving of love. I needed a triumph of my own and the requirement was immediate, but I had only been given 5 minutes to speak. Only one thing for it, get some speed up and, yes, my talk was completed in 4 minutes 45 seconds: a 'personal best'! Never before had I managed to shave 15 seconds off an attempt at a 5-minute talk. However, my pleasure in the achievement was soon dented. Apparently, with only a little extra training, the audience felt that the substance of my presentation need only have taken 30 seconds...

'HOTSPUR'

Male Hypogonadism: Basic, Clinical and Therapeutic Principles

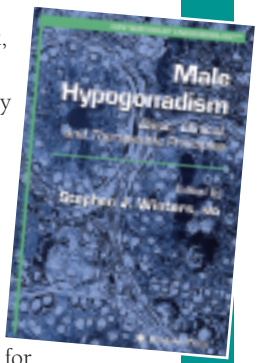
Ed Stephen J Winters, Humana Press, 2004, 396pp, $135, ISBN: 1-58829-131-6

This volume, part of the Contemporary Endocrinology Series, is aimed at a wide audience encompassing both basic scientists and practising clinicians.

The first three chapters describe the neuroendocrine control of testicular function (Winters and Dalkin), Leydig cell function in man (Dong and Hardy), and the regulation of spermatogenesis in higher primates (Marshall). Meanwhile, chapters 4-9 deal with the various causes of classical hypogonadism, starting with normal and delayed puberty (Dunkel), congenital hypogonadotrophic hypogonadism (Pitteloud and Crowley), hypogonadism due to gonadotrophin subunit and gonadotrophin receptor mutations (Huhtaniemi), hypogonadism in males with congenital adrenal hyperplasia (Otten *et al.*), male secondary non-inherited hypogonadism (Colao *et al.*), and Klinefelter's syndrome (Amory and Bremner). Inevitably, they are not invariably up to date, and the mutations within the FGFR1 gene and inherited forms of hypogonadotrophic hypogonadism do not get a mention.

Subsequent chapters deal with cryptorchidism (Lee *et al.*), hypogonadism in men with HIV-AIDS (Bhasin), hypogonadism in renal failure (Liu and Handelsman), male hypogonadism resulting from cancer and cancer treatment (Howell and Shalet), age-related hypogonadism (Veldhuis *et al.*), environmental causes of testicular function (Sharpe), exercise and hypogonadism (Hackney and Dobridge), testosterone, SHBG and the metabolic cardiovascular syndrome (Zmuda and Winters), androgen replacement therapy in hypogonadism (Wang and Swerdloff) and, finally, stimulation of spermatogenesis in hypogonadotrophic men (Depenbusch and Nieschlag).

The individual chapters are generally very intelligible, with the notable exception of one entitled 'an ensemble perspective of aging related hypoandrogenism in man'. The cumbersome title is every bit a taster of what follows: a hybrid section, partly mathematical, partly philosophical. The reader will come away with a feeling of inadequacy.



This chapter is not a good advert for the book, which in general is an enjoyable read, written by authorities in their areas, and mostly of a high quality. The breadth of this book is impressive indeed, and references are up to date. It constitutes an important thesaurus of information for those with a penchant for andrology, or who simply want to grasp the essentials of this important topic.

PIERRE BOULOUX

Hot Topics

More of the most recent research highlights from the Society's journals brought to you by Jolene Guy, Paul Ashton, Mona Munonyara and Stephanie Barber.

Osteoblast impact of rosiglitazone

The insulin-sensitising thiazoledinediones (TZDs), especially rosiglitazone, are commonly used in patients with type 2 diabetes mellitus. Soroceanu and co-workers now suggest that rosiglitazone has a negative impact on bone remodelling, by promoting osteoblast and osteocyte apoptosis.

While confirming previous findings that longitudinal treatment with rosiglitazone leads to bone loss in mice, they have demonstrated that 3-month oral treatment with rosiglitazone decreases osteoblast/osteocyte number and activity by decreasing Bcl-2 expression. This ultimately leads to lower rates of bone formation and decreased trabecular bone volume and bone mineral density. The study reports that mice in the rosiglitazone-treated and control groups were healthy and gained weight during the 3-month period, indicating that neither poor health nor nutritional deficiency were responsible for bone changes.

These findings raise concerns that the long-term use of TZDs in patients with type 2 diabetes or other insulin-resistant states may lead to decreased bone strength and a greater chance of fragility fractures. **JG**
(See the full article in Journal of Endocrinology ***183(1)****, October 2004)*

ER in mammary fibroblasts

Oestrogen receptor (ER)-α and ER-β are important in the developing mammary gland. In particular, in rodents, stromal ER-α is known to mediate signals that induce the release of growth factors, which in turn stimulate epithelial proliferation. However, the expression profile of these receptors in the stroma of the adult human breast is unclear. Palmieri and co-workers have now analysed the expression patterns of ER-α and ER-β in human breast tissue and in purified normal and malignant stromal fibroblasts.

Their findings clearly demonstrate that ER-β and its splice variants, but not ER-α, are expressed in both healthy and malignant fibroblasts. Further analysis revealed that release of fibroblast growth factor-7 (known to stimulate epithelial cell proliferation in the mammary gland) is induced by the ER-β-specific ligand, BAG, but not the high-affinity ER-β ligand, oestradiol.

These findings challenge current understanding of the role of ER-α in mediating the effects of oestrogen in adult human breast fibroblasts, and imply that ER-β and its variants may be important in cells where ER-α is absent. **PA**
(See the full article in Journal of Molecular Endocrinology ***33(1)****, August 2004)*

NMU-2 receptor variants and obesity

Neuromedin U (NMU) has been implicated in the modulation of appetite. Central administration suppresses food intake via the G-protein coupled NMU-2 receptor (NMU2R), which is expressed in known hypothalamic feeding centres.

In this study, Bhattacharyya and colleagues screened 96 patients with severe early-onset obesity for the NMU2R gene, to identify potential mutations associated with obesity. Though two different isoforms of the NMU2R were found, there was no correlation with obesity. As these sequence variants are present in Asian, European and African-American populations, the authors conclude that they were generated by a mutational event at least 100 000 years ago.

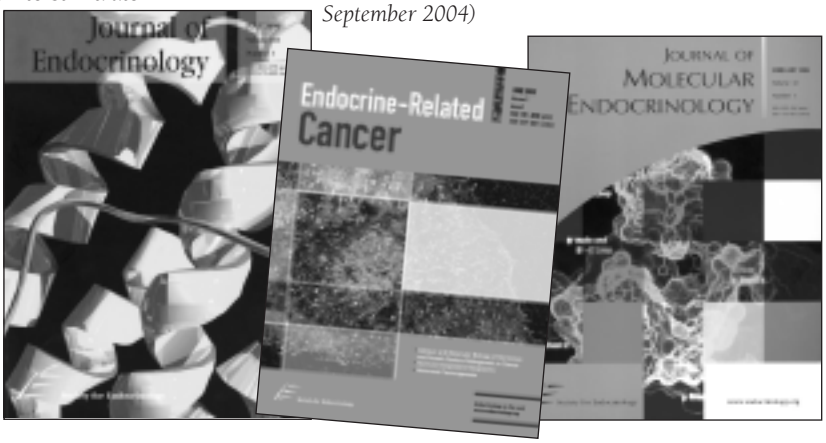
Although there is no evidence that genetic variation at the NMU2R locus influences obesity-related traits in man, further studies with larger populations are needed to understand the variants' roles. **MM**
(See the full article in Journal of Endocrinology ***183(1)****, October 2004)*

Targeting telomerase in prostate cancer

Prostate cancer, the leading cause of cancer-related deaths in men, is most effectively treated by androgen ablation. However, the emergence of androgen-independent tumour cells that are insensitive to this treatment has increased the need for new strategies.

Telomeres are specialised heterochromatin structures, which act as protective caps on the ends of chromosomes. They normally shorten with each round of cell division until they reach a critically short length, at which point the cell leaves the cell cycle and no longer replicates. Telomerase is an enzyme which catalyses the synthesis of telomeric DNA, maintaining telomere length and inducing immortality in the cells that express it. Telomerase is not found in normal and benign prostate tissue samples, but is present in nearly all human cancer cells.

In this review, Biroccio and Leonetti summarise the most promising results achieved using anti-telomerase strategies in different tumours, by directly or indirectly targeting telomerase and telomeres. They conclude that the combination of such approaches with conventional chemotherapy could efficiently improve responses to treatment in the future. **SB**
(See the full article in Endocrine-Related Cancer ***11(3)****, September 2004)*



195th Meeting of the Society for Endocrinology and Endocrinology and Diabetes Day jointly with Diabetes UK

London, UK, 1-3 November 2004.

Contact: Juliet Need, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642248; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfeconference2004).

3rd EFES Czech-Hungarian-Polish-Romanian-Slovak Regional Postgraduate Course in Endocrinology

Prague, Czech Republic, 4-6 November 2004.

Contact: Michal Krsek, Galen-Symposium sro, U Zvonarky 14, 120 00 Prague 2, Czech Republic (Tel: +420-222-520843; Fax: +420-222-516013; Email: knesplova@gsymposium.cz).

Diabesity: Gene Background and Lifestyle

Rome, Italy, 6-7 November 2004.

Contact: Melania Manco, Scientific Secretary, European Chapter of the American College of Nutrition, Department of Internal Medicine, Catholic University, Largo Gemelli 8, 00168 Rome, Italy (Tel: +39-06-30154903; Fax: +39-06-3054392; Email: melania.manco@rm.unicatt.it; Web: www.nutrition-europe.org).

32nd Meeting of the British Society for Paediatric Endocrinology and Diabetes

Aberdeen, UK, 10-12 November 2004.

Contact: Tamara Lloyd, BioScientifica Ltd, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: + 44-1454-642231; Fax: +44-1454-642222; Email: tamara.lloyd@endocrinology.org; Web: www.bsped.org.uk).

54th Meeting of the British Thyroid Association

London, UK, 11 November 2004.

Contact: Mark Vanderpump, Department of Endocrinology, Royal Free Hampstead NHS Trust, Pond Street, London NW3 2QG, UK (Tel: +44-20-74726280; Fax: +44-20-74726487; Email: mark.vanderpump@royalfree.nhs.uk; Web: www.british-thyroid-association.org).

NAASO 2004

Las Vegas, NV, USA, 14-18 November 2004.

Contact: Shirley Ash, North American Association for the Study of Obesity (Email: sash@diabetes.org).

International Conference on Steroid Hormone Receptor Superfamily and Molecular Signaling

Kerala, India, 18-20 November 2004.

Contact: Raghava Varman Thampan, Rajiv Gandhi Centre for Biotechnology, Thycaud PO, Thiruvananthapuram 695014, Kerala, India (Tel: +91-471-2347975; Fax: +91-471-2348096; Email: steroidrgcb2004@yahoo.com).

National Osteoporosis Society: 10th Conference on Osteoporosis

Harrogate, UK, 28 November-1 December 2004.

Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: janet@janet-crompton.com; Web: www.nos.org.uk).

CSSAM/ISSAM North American Congress on the Aging Male

Vancouver, Canada, 2-5 February 2005.

Contact: Irwin Kuzmarov, CSSAM/ISSAM North American Congress on the Aging Male, Kenes International, 17 Rue du Cendrier, PO Box 1726, CH-1211 Geneva 1, Switzerland (Tel: +41-22-9080488; Fax: +41-22-7322850; Email: aging@kenes.com; Web: www.kenes.com/aging).

1st National Conference on Obesity and Health

Manchester, UK, 7-8 February 2005.

Contact: Hannah Leach, Index Communications Meeting Services, Crown House, 28 Winchester Road, Romsey SO51 8AA, UK (Tel: +44-1794-511331; Fax: +44-1794-511455; Email: ncoh@indexcommunications.com; Web: www.obesityandhealth.co.uk).

Society for Endocrinology Clinical Cases Meeting

London, UK, 16 February 2005.

Contact: Ann Lloyd, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: ann.lloyd@endocrinology.org; Web: www.endocrinology.org).

8th Mayo Clinic Endocrine Course

Kohala Coast, HI, USA, 27 February-5 March 2005.

Contact: William Young, Mayo Clinic, 200 First Street, Rochester, MN 55905, USA (Tel: +1-507-2842191; Fax: +1-507-2845745; Email: young.william@mayo.edu; Web: www.mayo.edu/cme).

5th European Congress on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis

Rome, Italy, 16-19 March 2005.

Contact: YP Communication, Boulevard G Kleyer 108, 4000 Liège, Belgium (Tel: +32-4-2541225; Fax: +32-4-2541290; Email: yolande@piettecommunication.com).

35th Congress of the International Union of Physiological Sciences

San Diego, CA, USA, 31 March-5 April 2005.

Contact: IUPS 2005, The American Physiological Society, 9650 Rockville Pike, Bethesda, MD 20814-3991, USA (Tel: +1-301-6347160; Fax: +1-301-6347241; Email: iups2005@the-aps.org; Web: www.iups2005.org).

Fertility 2005

Warwick, UK, 2-6 April 2005.

Contact: Debbie Walker, World Event Management, Summit House, Woodland Park, Cleckheaton BD19 6BW, UK (Tel: +44-1274-854100; Fax: +44-1274-854110; Email: fertility2005@world-events.com; Web: www.jointukfertility.co.uk).

BES 2005: 24th Joint Meeting of the British Endocrine Societies

Harrogate, UK, 4-6 April 2005.

Contact: British Endocrine Societies, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfe/confs.htm).

4th Congress of the Mediterranean Society for Reproductive Medicine (MSRM)

Cote d'Azur, France, 7-9 April 2005.

Contact: Dr Ashraf Samir, PO Box 125, Ibrahimieh, Alexandria 21321, Egypt (Tel: +20-3-3595043; Fax: +20-3-3595044; Email: drashraf@aast.edu).

1st International Congress on 'Prediabetes' and the Metabolic Syndrome: Epidemiology, Management and Prevention of Diabetes and Cardiovascular Disease

Berlin, Germany, 13-16 April 2005.

Contact: Kenes International, 17 Rue du Cendrier, PO Box 1726, CH-1211 Geneva 1, Switzerland (Tel: +41-22-9080488; Fax: +41-22-7322850; Email: prediabetes@kenes.com; Web: www.kenes.com/prediabetes).

ATA 2005: Horizons in Thyroidology

Baltimore, MD, USA, 15-17 April 2005.

Contact: American Thyroid Association, 6066 Leesburg Pike, Suite 650, Falls Church, VA 22041, USA (Tel: +1-703-9988890; Fax: +1-703-9988893; Email: admin@thyroid.org; Web: www.thyroid.org).

Diabetes UK Annual Professional Conference 2005

Glasgow, UK, 20-22 April 2005.

Contact: Conference Team (Tel: +44-20-74241156; Email: conferences@diabetes.org.uk).

16th IFCC-FESCC European Congress of Clinical Chemistry and Laboratory Medicine

Glasgow, UK, 8-12 May 2005.

Contact: EuroMedLab Glasgow 2005 (Tel/Fax: +44-141-4341500; Email: euromedlab2005@meetingmakers.co.uk; Web: www.glasgow2005.org).

6th Puberty Conference

Evian, France, 26-28 May 2005.

Contact: Catherine Hellstedt, Congrex Sweden AB, Karlavägen 108, PO Box 5619, SE-114 86 Stockholm, Sweden (Tel: +46-8-4596637; Fax: +46-8-6619125; Email: catherine.hellstedt@congrex.se; Web: www.congrex.com/puberty2005).

ECO 2005: 14th European Congress on Obesity

Athens, Greece, 1-4 June 2005.

Contact: Triaena Tours & Congress SA, Atchley House, 15 Messogion Ave, 115 26 Athens, Greece (Tel: +30-210-7499315; Fax: +30-210-7705752; Email: congress@triaenatours.gr; Web: www.eco2005.gr/index.html).

ENDO 2005

San Diego, CA, USA, 4-7 June 2005.

Contact: The Endocrine Society, 8401 Connecticut Avenue, Suite 900, Chevy Chase, MD 20815-5817, USA (Tel: +1-301-9410200; Fax: +1-301-9410259; Email: endostaff@endo-society.org; Web: www.endo-society.org/scimeetings).

21st Annual Meeting of the European Society of Human Reproduction and Embryology

Copenhagen, Denmark, 19-22 June 2005.

Contact: Bruno van den Eede, ESHRE Central Office, Van Akenstraat 41B, 1850 Grimbergen, Belgium (Tel: +32-2-2690969; Fax: +32-2-2695600; Email: eshre@pophost.eunet.be; Web: www.eshre.com).

2nd Joint Meeting of the European Calcified Tissue Society and the International Bone and Mineral Society

Geneva, Switzerland, 25-29 June 2005.

Contact: European Calcified Tissue Society, PO Box 337, Bristol BS32 4ZR, UK (Tel: +44-1454-610255; Fax: +44-1454-610255; Email: admin@ectsoc.org; Web: www.ectsoc.org).

Annual Meeting of the Bone and Tooth Society

Birmingham, UK, 4-5 July 2005.

Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: janet@janet-crompton.com; Web: www.batsoc.org.uk).

Society for Endocrinology Summer School 2005: Molecular Endocrinology Workshop

Durham, UK, 5 July 2005.

Contact: Ann Lloyd, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: ann.lloyd@endocrinology.org).

Society for Endocrinology Summer School 2005: Advanced Endocrine Course

Durham, UK, 6-7 July 2005.

Contact: Ann Lloyd, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: ann.lloyd@endocrinology.org).

Society for Endocrinology Summer School 2005: Clinicl Practice Day

Durham, UK, 8 July 2005.

Contact: Ann Lloyd, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: ann.lloyd@endocrinology.org).

INTRODUCING

a breakthrough treatment for acromegaly…

SOMAVERT®

(pegvisomant powder and solvent for solution for injection)

IGF-1 normalisation is within reach

Somavert® (pegvisomant) Prescribing Information.
Presentation: Somavert powder and solvent for solution for injection is supplied in vials containing 10mg, 15mg or 20mg of pegvisomant. After reconstitution, 1ml of solution contains 10mg, 15mg or 20mg of pegvisomant. **Indications:** Somavert is used in the treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise IGF-I concentrations or was not tolerated. **Dosage:** Adults including elderly: A loading dose of 80mg should be administered subcutaneously under medical supervision. Following this, 10mg reconstituted in 1ml of water for injections should be administered once daily. Dose adjustments should be based on serum IGF-I levels, measured every four to six weeks, and appropriate dose adjustments made in increments of 5mg/day in order to maintain the serum IGF-I concentration within the age-adjusted normal range. The maximum dose should not exceed 30mg/day. Children: The safety and effectiveness of Somavert have not been established. **Contra-indications:** Hypersensitivity to pegvisomant or any of the excipients. **Warnings and precautions:** Growth hormone-secreting pituitary tumours may sometimes expand, causing serious complications (for example, visual field defects). Treatment by Somavert does not reduce tumour size. All patients with these tumours should be carefully monitored. Serum concentrations of alanine aminotransferase (ALT) and aspartate transaminase (AST) should be monitored at four to six week intervals for the first six months of treatment with Somavert, or at any time in patients exhibiting symptoms suggestive of hepatitis. Evidence of obstructive biliary tract disease should be ruled out in patients with elevations of ALT and AST or in patients with a prior history of treatment with any somatostatin analogue. Administration of Somavert should be discontinued if signs of liver disease persist. In patients with diabetes mellitus, doses of insulin or hypoglycaemic medicinal products may need to be decreased. Patients should be advised to use adequate contraception if necessary. The use of Somavert in combination with other medicinal products for the treatment of acromegaly has not been extensively investigated. **Pregnancy and lactation:** Somavert is not recommended during pregnancy and lactation. **Interactions:** Interactions between Somavert and other medicinal products have not been evaluated in formal studies. Patients receiving insulin or oral hypoglycaemic medicinal products may require dose reduction of these therapeutic agents due to the effect of Somavert on insulin sensitivity. Somavert cross-reacts in commercially available growth hormone assays. Treatment should therefore not be monitored or adjusted based on serum growth hormone concentrations reported from these assays. **Side effects:** In clinical trials, for patients treated with Somavert, the majority of adverse reactions to Somavert were of mild to moderate intensity, of limited duration and did not require discontinuation of treatment. The most commonly reported adverse events considered related to Somavert occurring in ≥ 5% of patients with acromegaly during the clinical trials were injection site reactions 11%, sweating 7%, headache 6%, and asthenia 6%. Most injection site reactions characterised as localised erythemas and soreness, spontaneously resolved with local symptomatic treatment, while therapy continued. The development of isolated low-titre anti-growth hormone antibodies was observed in 16.9% of patients. The clinical significance of these antibodies is unknown. **Overdose:** There is limited experience of overdosage with Somavert. In the case of overdose, Somavert should be discontinued and not resumed until IGF-I levels return to within or above the normal range. **Legal category:** POM. **Date of revision:** March 2004. **Package quantities, Marketing Authorisation numbers and basic NHS price:** Somavert 10mg, (30 vials of powder & 30 vials of solvent), EU/1/02/240/001, £1500. Somavert 15mg, (30 vials of powder & 30 vials of solvent), EU/1/02/240/002, £2250. Somavert 20mg, (30 vials of powder & 30 vials of solvent), EU/1/02/240/003, £3000 & (1 vial of powder & 1 vial of solvent), EU/1/02/240/004, £100. **Marketing Authorisation Holder:** Pfizer Limited, Sandwich, Kent CT13 9NJ, United Kingdom. Somavert is a registered trade mark. Ref: SV 1_3. Further information is available on request from: Medical Information Department, Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey KT20 7NS. **Date of Preparation:** April 2004. **Item code:** SOM 124.

Pfizer

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